ON-FLOW PREHEATING IN NMR MEASUREMENTS

BACKGROUND OF THE INVENTION

This invention is in the technical field of nuclear magnetic resonance (NMR) measurements. More particularly, the invention relates to a method and apparatus for controlling temperature of liquid samples before and during an NMR measurement in an NMR spectrometer.

In high throughput NMR techniques, saving time is of paramount importance. Most high throughput NMR techniques use a flow probe, and a liquid sample is pushed into the NMR probe through a tubing with a small inner diameter to an active region, or a flow cell of the probe. Thereafter, precious time is lost in heating the sample to thermal equilibrium. The time to reach thermal equilibrium in a currently used NMR probe of a prior art design may be two minutes or longer, depending upon the desired end temperature.

SUMMARY OF THE INVENTION

It is a general object of this invention to improve the throughput time in NMR measurements.

It is a particular object of this invention to provide a method and apparatus for preheating a liquid sample being pushed into an NMR probe without disturbing the magnetic field for the measurement.

For carrying out an NMR experiment according to the present invention, the inlet tubing through which a sample liquid flows from a sample source into a flow cell is provided with a heater comprising a twisted-pair wire tightly wrapped around helically such that the sample liquid is preheated as it flows into the flow cell and hence that the time taken for it to reach thermal equilibrium is reduced. The use of a twisted-pair wire as a heater minimizes the effect of induced magnetic field. A process control device, commercially available, may be used to monitor and control the temperature of the inlet tubing and thereby controlling the electric current through the heater such that the temperature can be maintained at a desired level.

BRIEF DESCRIPTION OF THE DRAWING

Fig. 1 is a schematic view of an NMR probe embodying this invention set for an NMR experiment.

Fig. 2 is a schematic external view of the components of the NMR probe shown in Fig. 1.

Figs. 3, 4 and 5 are diagrams of spectra of NMR signals collected at different times after a sample liquid is injected into an NMR probe of this invention by varying the temperature of the preheating element and the amount of injected sample liquid.

DETAILED DESCRIPTION OF THE INVENTION

Fig. 1 shows the general setup for an NMR experiment according to this invention. Numeral 10 indicates an NMR probe including a flow cell 12 and an inlet tubing 14 serving as a liquid transfer line through which a sample liquid is to flow into the flow cell 12 from a sample source 20 which may be a high pressure liquid chromatography (HPLC) system or a liquid handling robot of a known kind. The NMR probe 10 is positioned inside a high-field magnet 30 such that the flow cell 12 is centered in the active regions of its coils necessary for NMR spectroscopy.

As shown more clearly in Fig. 2, the inlet tubing 14 to the flow cell 12 has a twisted-pair wire 15 tightly and helically wrapped around and connected to a power supply source (not shown) so as to serve as its heater. Fittings of a known kind are used to connect the flow cell 12 with the inlet tubing 14.

The twisted-pair wire 15 is used as the heater for the inlet tubing 14 in order to reduce the induced magnetic field caused by the current traveling through the heater wire such that the critically important homogeneity condition for the high-field magnet 30 can be maintained.

Numeral 17 indicates a thermocouple for sensing the temperature at the inlet tubing 14. Although not shown, a commercially available external temperature controller is provided to control the temperature of the inlet tubing 14 according to the temperature sensed by the thermocouple 17.

A method of NMR experiment embodying this invention is therefore characterized as including a step of preheating a sample liquid which passes through the inlet tubing 14 into the flow cell 12 of the NMR probe 10. As the sample liquid flows from the sample source 20, it begins to be heated inside the inlet tubing 14 serving as the transfer line, or just as it enters the probe 10. Because the liquid tends to be a small flowing stream of liquid traveling at rates between 1-4ml/minute, it can be preheated in the inlet tubing 14.

It is well known in electronics that when a current is streaming through a coiled wire, a magnetic field is thereby induced. Since the preheating process is carried out by means of a heater comprised of a twisted-pair wire 15, two equal and opposite magnetic fields are produced which serve to cancel each other and hence do not disturb the overall homogeneity of the magnetic field necessary for high quality NMR spectroscopy.

The temperature at the inlet tubing 14 is monitored and the current for the heater is controlled according to the temperature sensed by the thermocouple 17.

The invention is described next by way of experimental results obtained by using a model probe produced as embodying this invention. A water sample containing 10% heavy water, sodium chloride and disodium dihydrogen ethylenediaminetetraacetate (EDTA) was used for the testing. This sample has temperature-dependent chemical shifts which were used as markers. As the sample warms, the resonance frequency of the EDTA changes relative to the water signal since the spectrometer is locked on the heavy water. Once the resonance frequency stops changing, the sample may be considered to be at thermal equilibrium. Thus, the time it takes to reach a state of thermal equilibrium can be determined. Figs. 3, 4 and 5 show that preheating of the sample liquid significantly reduces the time required for thermal equilibrium inside the active region of the probe 10, or the flow cell 12.

Fig. 3 shows the spectra of temperature sensitive NMR signals collected immediately after 1ml of fluid was injected into the flow probe without preheating. The frequency of the signal changes as the temperature of the sample is equilibrating from 22°C to 48°C. The liquid in the flow cell is considered equilibrated when the frequency of the signal becomes stable. The time to reach equilibrium in this experiment was 95 seconds.

Fig. 4 shows the spectra obtained by setting the preheating temperature to 48°C. The NMR measurements of temperature-sensitive signals were started immediately after 0.5ml of the fluid was injected into the flow probe with the preheated inlet tubing 14. The equilibration time was significantly reduced to approximately 5 seconds without compromising field homogeneity.

Fig. 5 shows the effects of preheating after 1.0ml of fluid was injected with the preheating temperature set also at 48°C. The equilibration time is seen to have been reduced approximately to 30 seconds. The user may adjust the temperature of the preheating according to the injected volume of the sample to minimize the equilibration time since the equilibration time depends not only on the temperature of the preheating but also on the amount of the sample fluid which is injected.